



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Provisional Application of:  
Joseph Artiss, et al.

Application No.: 10/628,475

Filed: July 29, 2003

Art Unit: 3765

For: COMPOSITIONS COMPRISING DIETARY  
FAT COMPLEXER AND METHODS FOR  
THEIR USE

Examiner: Not Yet Assigned

**APPLICANTS' DETAILED DISCUSSION OF THE REFERENCES**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

In accordance with 37 C.F.R. §1.102(d) and MPEP §708.2 (VIII) applicants provide herewith a detailed discussion of the references identified in the pre-examination search and point out with particularity how the claimed invention is patentable over those references.

**Non-US References**

Japanese Patent Application No. 05113603 (Publication No. 08187060 inventor Matsushima Itsuro), like Japanese Patent Application No. 5-164024 *infra*, assays the effect of a mixture of about 15%  $\alpha$ -cyclodextrin and 1.5% linolenic acid on weight gain in humans. The application discloses that subjects ingesting the  $\alpha$ -cyclodextrin/linolenic acid compositions in an amount based on their body weight, such that the daily dose of the composition was about 0.015g/kg body weight three times a day, which is 1.37g/91kg (200lb) individual three times per day, (which corresponds to 4.11 g of total composition per day or 0.62 g  $\alpha$ -cyclodextrin per day (0.21g/meal) and 0.068 g linolenic acid per day (0.023 g/meal)), displayed a significant increase in weight loss as compared to subjects who did not ingest the combination. However, this

application did not assay the effect of  $\alpha$ -cyclodextrin alone or linolenic acid alone nor did they disclose the fat content of the diets. Thus this application does not teach or suggest that  $\alpha$ -cyclodextrin forms complexes with neutral fats, nor does the application teach or suggest reducing the bioavailability of fat in a food product by determining the amount of fat in a food product and then adding  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to 1:3.

Japanese Patent Application No. 05164024 (Publ. No. 06-343419; inventor Matushima Masa) assays the effect of a mixture of about 15%  $\alpha$ -cyclodextrin and 1.5% linolenic acid on weight gain in humans. The applications disclose that subjects who ingested the  $\alpha$ -cyclodextrin/linolenic acid compositions in an amount based on their body weight such that the daily dose of the composition was about 0.015g/kg body weight three times a day which is 1.37g/91kg (200lb) individual three times per day, which corresponds to 4.11 g of total composition per day or 0.62 g  $\alpha$ -cyclodextrin per day (0.21g/meal) and 0.068 g linolenic acid per day (0.023 g/meal)), displayed a significant increase in weight loss as compared to subjects who did not ingest the combination. However, this application did not assay the effect of  $\alpha$ -cyclodextrin alone or linolenic acid alone nor did it disclose the fat content of the diets. The 5-164024 application does not teach or suggest that  $\alpha$ -cyclodextrin forms complexes with neutral fats, nor does the reference teach or suggest the addition of  $\alpha$ -cyclodextrin to a consumable fat-containing food product to reduce the bioavailability of fat in the food product or suggest  $\alpha$ -cyclodextrin be added in a specific amount sufficient to obtain a ratio of  $\alpha$ -cyclodextrin to fat of about 1:20 to 1:3.

Japanese Unexamined Patent Application No. H6-153861 (Patent Application No. H4-333575; inventor Tadashi Fujita) relates to compositions containing branched or unbranched  $\alpha$ -cyclodextrin,  $\gamma$ -linolenic acid, and a peptide having activation functionality. The disclosed compositions contain, in varying quantities by weight,  $\alpha$ -cyclodextrin,  $\gamma$ -linolenic acid, and a peptide having activation functionality. The applicants state it is essential to combine all three compounds to obtain a synergic action, by using 0.5-50 weight part of  $\gamma$ -linolenic acid and 10-1000 weight part of the peptide for each 100 weight part of  $\alpha$ -cyclodextrin. This application discloses supplementing the diet of rats with particular total amounts of linolenic acid and/or  $\alpha$ -

cyclodextrin and/or a peptide hydolysate by gavaging rats with wheat starch compositions comprising either 0.9%w/w linolenic acid alone, 9% w/w  $\alpha$ -cyclodextrin alone, or 100%w/w of a compositions of small molecular weight hydrolytes of a larger molecular weight protein, or with compositions comprising combinations of the three components. The rats were allowed to feed ab libitum but the fat content of the food was not disclosed nor did the inventors adjust the amount of cyclodextrin administered to the rats based on the amount of fat in the rat food. Thus the 6-153861 patent does not suggest or teach a method to reduce the bioavailability of fat in a fat-containing food product by determining the amount of fat in the food product and adding  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20-1:3.

Japanese Patent Application No. 05298849 (Patent Application No. 07 115934; inventor Shiozu Tatsuzo) assays the effects of linolenic acid and  $\alpha$ -cyclodextrin on weight gain in rats. This application reports that rats fed diets comprising either 16%  $\alpha$ -cyclodextrin or 1% linolenic acid gain weight approximately the same as rats fed a control diet. This Japanese application discloses that rats fed diets comprising a combination of 14%  $\alpha$ -cyclodextrin and 2% linolenic acid incur significant weight loss. The fat content in the rat diets was not disclosed. The 7-115934 application does not teach or suggest the use of cyclodextrin to reduce the bioavailability of fat in a fat-containing food product, nor does the reference teach or suggest determining the amount of fat in a food product and then adding  $\alpha$ -cyclodextrin to the fat-containing food products such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20-1:3.

Japanese Unexamined Patent Application No. S60-94912 (Patent Application No. S58-201033; inventor Masashige Suzuki et al.) relates to neutral fat-reducing compositions containing cyclodextrin, specifically compositions containing  $\alpha$ -,  $\beta$ -, and  $\gamma$ -cyclodextrin either alone or in specific ratios. The compositions contained from 10% to 40%  $\alpha$ -cyclodextrin by total weight. The cyclodextrins are not added based on the amount of fat in the food product. The reference does not teach or suggest that  $\alpha$ -cyclodextrin forms complexes with fat and does not suggest a method for reducing the bioavailability of fat in a food product by determining the amount of fat in the food product and adding  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20-1:3.

Japanese Unexamined Patent Application No. 62-011072 (Patent Application No. S60-149725; inventor Hitoshi Saito) relates to a food containing  $\alpha$ -cyclodextrin and  $\gamma$ -linolenic acid, preferably in specific ratios, e.g. 100 parts  $\alpha$ -cyclodextrin and 5-10 parts  $\gamma$ -linolenic acid. The inventors state that for this invention it is essential to combine the two compounds. This application analyzes the effect of linolenic acid in combination with  $\alpha$ -cyclodextrin on weight gain in rats. This application reports that a diet comprising 14% w/w  $\alpha$ -cyclodextrin has little effect on weight gain in rats while the combination of 14% w/w  $\alpha$ -cyclodextrin and 0.5%w/w linolenic acid produces significant weight loss. The reference does not disclose the composition of the rat food and thus does not teach the fat content of the food. Therefore, the reference does not teach or suggest reducing the bioavailability of fat in a fat-containing food product by determining the amount of fat in a fat-containing food product and adding  $\alpha$ -cyclodextrin to fat-containing food product such that the ratio of  $\alpha$ -cyclodextrin to the fat is about 1:20 to 1:3.

Japanese Public Patent Disclosure Bulletin No. Sho 62-81310 (Patent Application No. 60-219720; inventor Suzuki et al.) describes a drink material which includes a triglyceride, which contains gamolenic acid and gamolenic acid esters. The triglycerides with gamolenic acid are enclosed in cyclodextrin to overcome the difficulty in mixing the compounds with the drink material (page 6) by adding the triglycerides/gamolenic acid/gamolenic acid esters in a fixed amount to a saturated or supersaturated solution or slurry of cyclodextrin. The cyclodextrin encapsulated material is isolated and subsequently added to the drink in the amount of 0.01-1% by weight. The reference does not suggest or teach a method to reduce the bioavailability of fat after ingestion of a fat-containing food product. The reference also does not disclose the addition to foods or food products of  $\alpha$ -cyclodextrin in specific ratio to the fat content of a food or food product, such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20-1:3.

Japanese unexamined Patent Application No. H7-115935 (Patent Application No. H5-298850; inventor Tatsuzo Shiozu) describes a diet food containing a barley green element,  $\alpha$ -cyclodextrin, and  $\alpha$ -linolenic acid in specific ratios by weight, preferably 50-80 weight parts, 20-40 weight parts and 0.5-20 weight part respectively. The three elements are contained at specific ratios in various foods and food additives. The H7-115 935 application teaches that the three elements act synergistically to prevent obesity and weight gain. The compound is fed to rats but the

fat content of the rat diet is not disclosed. Furthermore, the application does not disclose the effect of  $\alpha$ -cyclodextrin alone. The application does not disclose a method for reducing the bioavailability of fat in a fat containing food product comprising determining the amount of fat in the food product and adding a sufficient amount of  $\alpha$ -cyclodextrin to the food product such that the ratio of  $\alpha$ -cyclodextrin to fat of about 1:20-1:3 based on the fat content of a food product.

Japanese Public Patent Disclosure Bulletin No. Hei 2-261334 (Patent Application No. Hei 1-82468; inventor Osami Nishimura) relates to an oil-in-water and fat emulsion for use in cakes to improve the melt-in-your-mouth aspect of sponge cake. The emulsion contains 1 to 10% by weight cyclodextrin, 0.05 to 5% by weight of at least one kind of common salt, and preferably 0.05 to 5% by weight of a polyglycerol fatty acid ester. The examples disclose an emulsion of corn oil, water,  $\beta$ -cyclodextrin, sodium citrate, and table salt. The reference teaches the use of the emulsion composition to improve the melting of soft and fine cakes having large specific volumes and to simplify the making of cakes having a moist texture. The reference does not teach or suggest a method for reducing the bioavailability of fat in a consumable fat containing food product by determining the amount of fat in the food product and then combining the food product with an amount of  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to about 1:3 wherein the  $\alpha$ -cyclodextrin is not removed prior to consumption.

Japanese Public Patent Disclosure Bulletin No. SH060-49752 (Patent Application No. SHO 58-156288; inventor Toshiaki Kirino) refers to a nutritional food supplement comprised of royal jelly and octacosanol. In one example, the application discloses combining 50g of a cyclodextrin solution (cyclodextrin 23%, other sugars 52%, water 25%) to 50g of an oil solution (10 grams of 50% octacosanol added to 90 grams of cottonseed oil), where 50 grams of the resulting aqueous paste are added to 450 grams of royal jelly and mixed. The reference does not teach or suggest a method as claimed in the present application, i.e., the use of cyclodextrin to reduce the bioavailability of fat-containing food. The reference also does not teach or suggest the addition of  $\alpha$ -cyclodextrin to foods or food products, such that the ratio of  $\alpha$ -cyclodextrin to fat which a subject desires to prevent from being absorbed is about 1:20-1:3 in the food products.

Japanese Laid Open Application No. SHO 52-10448 (Patent Application No. SHO 50-86429; inventory Toyooki Yoneda) uses a cyclodextrin as an emulsifier to combine with water and

oil/fat. In contrast to applicant's invention, this application uses cyclodextrin to deliver fat to the gastrointestinal tract thereby enhancing its bioavailability, wherein applicants use  $\alpha$ -cyclodextrin to reduce the bioavailability of fat. The inventors state "oils and fats are inherently difficult to digest, previously mentioned emulsification and flavor enhancers have been used to improve edibility" (page 3, third full paragraph). This Japanese application also states "this invention is a unique manufacturing method for processed edible oils and fat products, the emulsifier of which is a triglyceride (fatty-acid and glycerin) type cyclodextrin inclusion compound." (page 4 first full paragraph). Thus in contrast to applicants' invention which reduces the bioavailability of fat in a food product, the methods of the methods of this application are designed to increase the availability of fat/oils. As such SHO 50-86429 does not teach or suggest the methods of this invention.

European Patent Application EP 1 120 046 A1 (the EP application) discloses a pet food comprising a cyclodextrin such as  $\beta$ -cyclodextrin and a method for suppressing an increase in body weight of a pet by feeding the pet food to the pet such that the ingested amount of  $\beta$ -cyclodextrin ranges from 0.1 to 5g per 1kg of body weight per day.  $\beta$ -cyclodextrin and fat are present in independently varying amounts in the described pet food (see, e.g., abstract). The EP application does not describe a pet food comprising  $\alpha$ -cyclodextrin. The EP application does not teach or suggest a method for reducing the bioavailability of fat in a consumable fat containing food product by determining the amount of fat in the food product and then combining the food product with  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to about 1:3 wherein the  $\alpha$ -cyclodextrin is not removed prior to consumption. Nor does the EP application describe the method claimed, i.e., a method for promoting weight loss in a subject by administering  $\alpha$ -cyclodextrin to said subject such that the ratio of  $\alpha$ -cyclodextrin and ingested fat that the subject desires to prevent from being absorbed is about 1:20 to 1:3.

### **US Patent References**

U.S. Patent No. 4,800,573 discloses a process for eliminating cholesterol from fatty substances of animal origin using cyclodextrins. The process as disclosed requires that the fatty substance be kept in a liquid state, to which cyclodextrin is added, forming cyclodextrin/cholesterol complexes that will separate in an aqueous phase. The complexes are then separated by

entrainment in water and separation of the aqueous phase. In contrast, the methods as taught in this application do not remove cyclodextrin complexes from the consumable food products. The '573 patent does not teach that  $\alpha$ -cyclodextrin will form complexes with fat, nor does it teach or suggest a method for reducing the bioavailability of fat in a consumable fat containing food product by determining the amount of fat in the food product and then combining the food product with  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to about 1:3 wherein the  $\alpha$ -cyclodextrin is not removed prior to consumption.

U.S. Patent No. 5,571,554 relates to a process for reducing the triglyceride content of egg yolk and egg yolk-containing products. The '554 patent discloses an extraction technique where cyclodextrin is used to reduce the quantity of triglycerides in egg yolk and egg yolk-containing products by diluting egg yolk with water or an aqueous salt solution to produce a mixture, adding at least one cyclodextrin, separating off the cyclodextrin/triglyceride complex from the mixture and then separating off the added water or aqueous salt solution (col. 1, line 62 to col. 2, line 2). The amount of cyclodextrin added to the diluted egg yolk is based on the weight of the undiluted yolk and not based on the amount of fat in the yolk. The amount of cyclodextrin is greater than 3% by weight and the patent discloses that preferably  $\alpha$ -cyclodextrin is used in an amount that is 45-80% by weight and  $\beta$ -cyclodextrin is used in an amount that is 45-150% by weight. Applicants methods relate to a method for reducing the bioavailability of fat in a food product by combining the food product with  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin and fat is 1:20 to 1:3. In contrast to the 5,571,554 patent, applicants do not remove cyclodextrin or cyclodextrin/triglyceride complexes from the consumable food products prior to consumption.

U.S. Patent No. 5,560,950 discloses a method for reducing the free fatty acid content of frying fats and oils by adding cyclodextrin and a powdered absorbent to heated fat or oil, allowing the resulting slurry to react preferably for about one and one half hours, and then separating the cyclodextrin and absorbent material and free fatty acid from the heated fat or oil, thereby reducing the free fatty acid content (col. 3, line 39 to col. 4, line 5). Applicants methods do not remove cyclodextrin or cyclodextrin complexes from the consumable food products and thus do not produce a product with reduced levels of free fatty acids. This patent does not teach or suggest that the cyclodextrin will form complexes with triglycerides and thus does not teach or

suggest applicants' method for reducing the bioavailability of fat in a fat-containing consumable food product.

U.S. Patent No. 5,189,149 relates to a method for the production of complexes of long chain polyunsaturated fatty acids, their salts and esters, with cyclodextrin and to the resulting complexes. Complexes are formed by mixing an aqueous solution of cyclodextrin with the active oleaginous substance (e.g. various types of fish oils, vegetable oils and long chain polyunsaturated fatty acids, their salts and alkyl and glycerol esters,) for 1-24 hours to form complexes which precipitate in a solid, crystalline form which are separated and recovered from the oleaginous substance and dried (col. 2, lines 24-33). The complexes are defined as inclusion compounds of long chain polyunsaturated substances enclosed in the hydrophobic cavities of the cyclodextrin (col. 3, lines 30-34). The concentration of oleaginous substance in the complex is higher than 18% by weight (col. 2, lines 39-42). The '149 patent states that the complexes can be used to prepare a variety of compositions with various pharmaceutical forms such as tablets, capsules, syrups, etc. However, the '149 patent only describes the formation of complexes of cyclodextrin and fatty acids; it does not disclose that  $\alpha$ -cyclodextrin forms complexes with fat. Nor does the '149 patent teach or suggest the method claimed, i.e., a method for reducing the bioavailability of fat in a consumable fat containing food product by determining the amount of fat in the food product and then combining the food product with  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to about 1:3 wherein the  $\alpha$ -cyclodextrin is not removed prior to consumption.

U.S. Patent 5,232,725 relates to an animal fat material particularly butter, dairy cream, anhydrous dairy fat, suet and lard having reduced levels of cholesterol and free fatty acids and to a process for reducing the cholesterol and free fatty acids in an animal fat material. The process comprises contacting cyclodextrin and fat in the presence of water, then separating the cyclodextrin cholesterol or free fatty acid complexes from the fat. Unlike the method claims of this application, the '725 patent teaches one to mechanically separate the complexes of cyclodextrin and cholesterol and free fatty acids from an animal fat material prior to consumption to produce an animal fat material with reduced levels of cholesterol and free fatty acids (see e.g., Abstract and Col. 2, lines 12-13). U.S. 5,232,725 does not describe applicants'

claimed method, i.e., a method for reducing the bioavailability of fat in a consumable fat containing food product by determining the amount of fat in the food product and then combining the food product with  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to about 1:3 wherein the  $\alpha$ -cyclodextrin is not removed prior to consumption.

U.S. Patent No. 5,264,226 discloses methods for preparing dairy products with a low content of sterols particularly cholesterol by contacting an oil-in-water emulsion comprising dairy fats with cyclodextrin in sufficient amount to form inclusion complexes with the sterols so that the latter can be extracted from the fat (see Abstract, Col. 3., lines 48-58). Similar to the foregoing patents and unlike the methods as claimed in this invention, the patent teaches the removal of the cyclodextrin complexes prior to consumption to produce a reduced cholesterol product. The methods as claimed in this application do not remove the  $\alpha$ -cyclodextrin from the food products and do not reduce the levels of cholesterol in the products.

U.S. Patent No. 5,264,241 teaches a process for manufacturing products, particularly dairy products, with a reduced content of sterols by contacting the starting materials with a sufficient amount of cyclodextrin to form inclusion complexes with the sterols present in the fat, inverting the oil-in-water emulsion and extracting the complexes in whole or part (see e.g. Abstract and Pat. No. 5,264,241, Col. 3, lines 45-58). Unlike the methods as claimed in this invention, the patent teaches the removal of the cyclodextrin complexes prior to consumption to produce a reduced cholesterol product. The methods as claimed in this application do not remove the  $\alpha$ -cyclodextrin from the food products and do not reduce the levels of cholesterol in the products.

U.S. Patent No. 5,738,898 relates to a process for reducing the cholesterol content of egg yolk by mixing cyclodextrin, a base, and water with the yolk. Like U.S. Patent No. 5,571,554, the '898 patent process requires separating cyclodextrin-cholesterol complexes from the egg yolk mixtures prior to ingestion (see e.g., col. 2, lines 29-39). The amount of cyclodextrin added to the yolk mixture is based on the amount of water in the mixture (col. 2, lines 33-35 and col. 3, lines 5-7). The '898 patent does not describe a method for decreasing the bioavailability of fat by determining the amount of fat in a food product and based on that amount adding in an amount of  $\alpha$ -cyclodextrin to form cyclodextrin-fat complexes. The methods as taught in this

application do not remove cyclodextrin or cyclodextrin/cholesterol complexes from the consumable food products.

U.S. Patent No. 5,824,354 relates to a process for reducing sterols and free fatty acids in liquefied animal fat by forming an oil-in-water emulsion of water, liquefied animal fat and cyclodextrin. The sterols and free fatty acids form complexes with the cyclodextrin during the processing and the complexes are separated from the emulsion by centrifugation. The fat produced by the process of this patent has a reduced sterol and free fatty acid content and the process results in a low residual cyclodextrin in the treated fat, below about 5ppm. Unlike the method recited in the claims of this application, the cyclodextrin is treated as a contaminant that should be removed from the fat (Col. 2., lines 37-39). Furthermore, unlike the methods recited in the claims of this application, the 5,824,354 patent does not teach determining the amount of fat in the food product and then combining the food product with  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to about 1:3.

U.S. Patent No. 6,129,945 also describes a method for removing free fatty acids and preferably cholesterol from liquid anhydrous animal fat by providing a reaction mixture of the free fatty acids in the liquid animal fat with a water solution of an alkali metal hydroxide at an elevated temperature to form soluble fatty acid salts (SFAS) then reacting the SFAS with an alkaline earth metal salt to form an insoluble fatty acid salt (IFAS) and then separating the IFAS from the reaction mixture to form a processed animal fat with reduced levels of free fatty acids. (see e.g. Abstract, col. 7, lines 23-36). In some embodiments  $\beta$ -cyclodextrin is added to also remove cholesterol along with the free fatty acids. The process simultaneously reduces cholesterol, melting point and free fatty acids in anhydrous milkfat using an aqueous liquid formula and  $\beta$ -cyclodextrin as a complexing agent for the cholesterol. U.S. Patent No. 6, 129, 945 states that their method selectively removes free fatty acids without precipitating or damaging the milk fat per se. Like U.S. Patent No. 5,232,725 this patent does not describe applicants' claimed method as described in the claims, i.e., a method for reducing the bioavailability of fat in a consumable fat containing food product by determining the amount of fat in the food product and then combining the food product with  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to about 1:3 wherein the  $\alpha$ -cyclodextrin is not removed prior to consumption.

U.S. Patent No. 5,217,734 relates to a method for normalizing a bird's feathers and to improve the color tone of the same (Col. 1, lines 21-25) and discloses a method for producing a PET bird feed additive comprising cyclodextrin and Dunaliella alga powder. The cyclodextrin is included in the bird feed to protect the  $\beta$ -carotene contained in Dunaliella alga powder from oxidation and to mask the characteristic odor of the alga powder (Col. 1, lines 49-55). 15-50 parts of cyclodextrin is used per 100 parts by weight of Dunaliella alga powder and 5-15 parts by weight of the additive is blended with a common bird feed. The reference does not teach or suggest a method for reducing the bioavailability of fat in a consumable fat containing food product by determining the amount of fat in the food product and then combining the food product with  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to about 1:3 wherein the  $\alpha$ -cyclodextrin is not removed prior to consumption

U.S. Patent No. 5,532,009 relates to a non-absorbable, non-digestible fat composition useful as a fat substitute in food and pharmaceutical compositions. The fat substitute is fortified with inclusion complexes of  $\beta$ -carotene (or similar carotenoids) and a  $\beta$ -cyclodextrin, or a  $\beta$ -cyclodextrin derivative, that are prepared and then added to the fat substitute. The  $\beta$ -cyclodextrin derivative is used to complex beta-carotene and to make it more bioavailable when added to an edible, non-digestible fat. The '009 patent does not teach or suggest that  $\alpha$ -cyclodextrin forms complexes with fats rendering them less bioavailable. The '009 patent describe the method as claimed, i.e., a method for reducing the bioavailability of fat in a consumable fat-containing food product by determining the amount of fat in the food product and then combining the food product with  $\alpha$ -cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20 to about 1:3 wherein the  $\alpha$ -cyclodextrin is not removed prior to consumption.

U.S. Patent No. 5,780,096 relates to a process for preparing a powdery chlorella extract purported to contain a higher concentration of substances for hastening the growth of an animal another active ingredients. Cyclodextrin is used in the process to produce the chlorella extract which can be used as health food in the form of, for example, capsules, biscuits, crackers, beverages and so forth, or as an additive for pet food. The reference does not teach or suggest the addition of any cyclodextrin to foods or food products and does not teach a method for reducing

the bioavailability of fat in a food product by combining  $\alpha$ -cyclodextrin with the food product such that the ratio of  $\alpha$ -cd to fat is 1:20 to 1:3.

U.S. Patent No. 5,894,029 relates to a method for producing a pet food which is touted to be a highly palatable, flavorful pet food snack which is low calorie, low fat, low cholesterol and highly nutritional. The pet food comprises a core matrix comprising approximately 70%-98.5% farinaceous material by weight of the snack, approximately 0.4% to 4.7% proteinaceous material by weight of the snack, and approximately 0.4 – 5% additives weight of the snack. The patentees cite cyclodextrin as one in a list of possible additives and state that cyclodextrin is added to the snack to selectively absorb aromatic compounds and then to release them in a controlled manner (Col. 4, lines 17-20). U.S. Patent No. 5,894,029 does not disclose any particular amount of cyclodextrin for addition to the core matrix. Unlike applicant's invention, the reference does not teach or suggest the use of  $\alpha$ -cyclodextrin to reduce the bioavailability of fat in a fat-containing food. The reference also does not teach or suggest the addition of  $\alpha$ -cyclodextrin to foods or food products such that the ratio of  $\alpha$ -cyclodextrin to fat in the food product is about 1:20-1:3.

U.S. Patent No. 5,989,583 discloses a method for producing dry solid lipid mixtures that have unexpectedly high drug-loading efficiency and enhanced oral bioavailability for lipophilic compounds (Col. 4 lines 20-53). The dry solid lipid mixture may comprise a cyclodextrin as a cryo-protectorant. The amount of cryoprotectorant added to the mixture is based on the total solids in the dry solid lipid mixture. The '583 patent does not describe a method for decreasing the bioavailability of fat by determining the amount of fat in a food product and based on that amount adding in an amount of  $\alpha$ -cyclodextrin to form cyclodextrin-fat complexes, nor does it describe the addition of cyclodextrin to fat-containing foods in an amount such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20-1:3.

U.S. patent application Serial No. US 2003/0190402 A1 published October 3, 2003, filed April 4, 2002. This application is not prior art to the invention as claimed. Applicants invented their invention prior to the filing date of this application.

**Journal Articles**

Anderson, G. H. *et al.*, “The Utilization of Schardinger Dextrins by the Rat” *Toxicology and Applied Pharmacology* 5, 257-266 (1963) relate experimental findings after feeding  $\alpha$ - and  $\beta$ -cyclodextrin to rats. Cyclodextrin or starch were labeled with a radioactive isotope of carbon, C-14, and dissolved in water and fed directly to rats. The authors conclude that the cyclodextrin is utilized by rats at a much lower rate than starch. The authors state rats maintained for 3 months on a diet containing 1% of the  $\alpha$ - or  $\beta$ -dextrins, showed growth curves and food efficiencies equal to the control diet containing no  $\alpha$ - and  $\beta$ -dextrins.” page 265. The composition of the diets was not disclosed. The reference does not teach or suggest the methods claimed in the present application, i.e., the use of cyclodextrin to reduce the bioavailability of fat-containing food. The reference also does not teach or suggest the addition of  $\alpha$ -cyclodextrin to foods or food products such that the ratio of  $\alpha$ -cyclodextrin to fat in the fat-containing food product is about 1:20-1:3.

Suzuki and Sato, “Nutritional significance of cyclodextrin: indigestibility and hypolipemic effect of  $\alpha$ -cyclodextrin” *J. Nutri. Sci. Vitaminol.* 31:209-223 (1985) report that rats fed diets comprising a mixture of n-dextrin and  $\alpha$ -,  $\beta$ - and  $\gamma$ - cyclodextrins (50:30:15:5% w/w) displayed weight loss significantly different from the control group only when at least 58.5% w/w of the diet consisted of the cyclodextrin mixture (see Figure 4) (18%  $\alpha$ -cyclodextrin, 25% total cyclodextrin). In contrast, applicants have found that significant weight loss can be obtained in subjects with much lower levels of  $\alpha$ -cyclodextrin if the subjects are consuming fat-containing diets and the ratio of ingested  $\alpha$ -cyclodextrin to ingested fat in the diet is sufficient to form complexes of fat and cyclodextrin. The reference does not teach or suggest determining the amount of fat in a food product and then adding  $\alpha$ -cyclodextrin to the fat-containing food products such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20-1:3. The reference also does not teach or suggest that cyclodextrin reduces the bioavailability of fat in fat-containing food product.

Kaewprasert, S. *et al.*, “Nutritional Effects of Cyclodextrins on Liver and Serum Lipids and Cecal Organic Acids in Rats” *J. Nutri. Sci. Vitaminol.* 47(5): 335-9 (2002) report findings from

experiments in which rats were fed diets of  $\alpha$ -,  $\beta$ -, and  $\gamma$ -cyclodextrin. Studies were designed to examine the comparative effects of cyclodextrins on lipid metabolism and cecal organic acid production. Rats were fed a diet of 5% cyclodextrin ( $\alpha$ -,  $\beta$ -, and  $\gamma$ -cyclodextrin) by weight, and cecal content and weight were analyzed. Kaewprasert et al. report that the weight of rats fed a diet comprising 5%  $\alpha$ -cyclodextrin were not significantly different than rats fed a control diet. Kaewprasert et al. disclose that the diets comprised cyclodextrin and fat in a ratio of 1:1.4. In contrast, this application teaches a method wherein  $\alpha$ -cyclodextrin is added to fat-containing food products such that the ratio of  $\alpha$ -cyclodextrin to fat is about a 1:20-1:3.

Szejtli, J., "Utilization of Cyclodextrins in Industrial Products and Processes" *J. Mater. Chem.*, 1997, 7(4), 575-587 relates the various uses of cyclodextrins in a number of industries and products in a review article format. The reference contains a brief summary of the use of cyclodextrins in foods and cosmetics. The authors state that low-cholesterol butter is produced in Belgium by mixing molten butter with  $\beta$ -cyclodextrin, "which does not react with triglycerides, but forms complexes with cholesterol" and "the  $\beta$ -CD complex is easily removable from the butter and the butter does not contain an CD" (page 583 right col.). The reference does not teach or suggest a method claimed in the present application, i.e., the use of cyclodextrin to reduce the bioavailability of fat in a fat-containing food product. The reference also does not teach or suggest the addition of  $\alpha$ -cyclodextrin to fat-containing food products such that the ratio of  $\alpha$ -cyclodextrin to fat is about 1:20-1:3.

Raben, Anne *et al.*, "Acetylation of or  $\beta$ -cyclodextrin addition to potato starch: beneficial effect on glucose metabolism and appetite sensations" *Am. J. Clin. Nutr.* 66:304-14 (1997) describe the use of two chemically modified starches; one is a 1-2% acetylated potato starch and a second is a starch enriched with 2%  $\beta$ -cyclodextrin. The reference does not discuss  $\alpha$ -cyclodextrin but uses  $\beta$ -cyclodextrin to delay gastrointestinal emptying and to produce a distal glucose absorption in small intestine. The authors do not disclose a relationship between  $\beta$ -cyclodextrin and dietary fat. The reference does not teach or suggest a method for reducing the bioavailability of a fat in a food product by determining the amount of fat in the food product and then adding an amount of any cyclodextrin such that the ratio of  $\alpha$ -cyclodextrin to fat was 1:20 to 1:3.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 06-2375, under Order No. AJC 201.1 US/10304772. A duplicate copy of this paper is enclosed.

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Respectfully submitted,

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